Halogenation of Keto Acid Phosphoranes: Synthesis of Halo Enol Lactones and Haloallenes

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Halolactonization of the keto acid phosphoranes **6a–f**, **40**, and **41** takes place with either Br_2 or SO_2Cl_2 and Et_3N to give the *E*- and *Z*-halo enol lactones **10–15**, **42**, and **43** in good yields. The cyclization proceeds via a halo phosphonium salt, e.g. **19**. Halo phosphonium salts yield a halo allene when cyclization is not favoured as in the formation of the bromoallenes **24** and **37**. The configuration of the halo enol lactones was determined by ^1H and ^{13}C NMR spectroscopy and via single-crystal X-ray determinations on **11a**, **14c**, and **42b**. The barrier to interconversion of the biphenyl conformations of the bromo enol lactones **42b** and **43b** was determined by ^1H NMR spectroscopy at elevated temperatures.

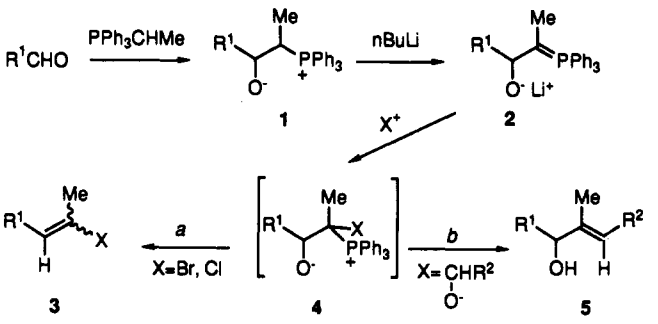
Introduction

The Wittig reaction has played a significant role in synthetic chemistry for several decades, even though the reaction mechanism is far from fully understood.[1] A useful extension of the classic Wittig reaction is the Schlosser modification, or α-substitution plus carbonyl olefination via β-oxido phosphorus ylides (SCOOPY) reaction.[2] In this reaction, an initially formed betaine **1**, derived from an aldehyde and a nonstabilized ylide, is treated with *n*-BuLi at low temperature to give a β-oxido ylide **2**. Reaction with a second aldehyde (R^2CHO) then gives the allylic alcohol **5**, stereoselectively, via the betaine **4** (Scheme I, pathway b). Halogen electrophiles,[2a,e,f] for example *N*-chlorosuccinimide, Br_2, or $FClO_3$, yield the analogous vinyl halides **3** (Scheme I, pathway a). The β-oxido ylide route to olefins allows the joining of three components in one operation, such that the oxygen of the first aldehyde is retained, whereas that of the second aldehyde is eliminated as triphenylphosphine oxide.[2a]

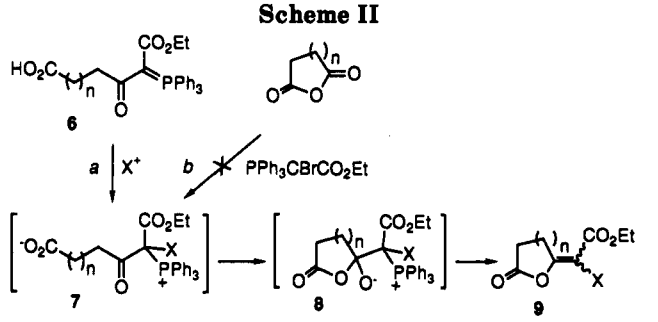
Here, we report[3] a modification (Scheme II, pathway a) to the SCOOPY reaction whereby the β-oxido ylide **2** (Scheme I) is bypassed and a betaine **8**, analogous to **4**, is produced on reaction of a keto acid phosphorane **6** with an electrophile. The normal sequence of the SCOOPY reaction is reversed in that the reaction of **6**, with Br_2 or SO_2Cl_2, promotes lactonization and hence the formation of the β-oxido group of **8**. Loss of triphenylphosphine oxide then occurs to give the halo enol lactone **9**, analogous to the vinyl halide **3**. The β-oxido group is generated prior to the addition of the electrophile in the standard SCOOPY reaction.

Halo enol lactones are found naturally,[4] and synthetic examples have gained considerable attention as mechanism-based inhibitors of serine proteases.[5] The keto acid phosphoranes **6** are also of interest as synthetic intermediates to hydrogen enol lactones,[6] allenes,[7] and acetylenes[8] and in the study of keto acid hydrogen bonding patterns.[9]

Scheme I



Scheme II



Results and Discussion

Methodology is given for the synthesis of the *E* and *Z* five-membered bromo enol lactones **10a** and **11a**, respectively (Table I). Br_2 and Et_3N were added to the keto acid phosphorane **6a**, in CH_2Cl_2, at 0 °C. The bromine decolorized instantaneously, and after 30 min, at 0 °C, the *E*- and *Z*-bromo enol lactones **10a** and **11a** were isolated

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(2) (a) Grieco, P. A.; Takigawa, T.; Vedananda, T. R. *J. Org. Chem.* **1985**, *50*, 3111. (b) Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *Tetrahedron Lett.* **1983**, *24*, 2477. (c) Corey, E. J.; Ulrich, P.; Venkateswarlu, A. *Tetrahedron Lett.* **1977**, 3231. (d) Schlosser M.; Christmann, F. K.; Piskala, A.; Coffinet, D. *Synthesis* **1971**, 29. (e) Corey, E. J.; Shulman, J. I.; Yamamoto, H. *Tetrahedron Lett.* **1970**, 447. (f) Schlosser, M.; Christmann, F. K.; Piskala, A.; Coffinet, D. *Synthesis* **1969**, 38.

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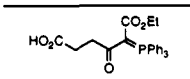
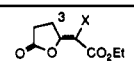
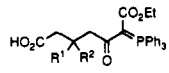
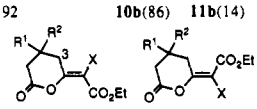
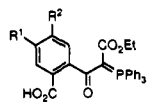
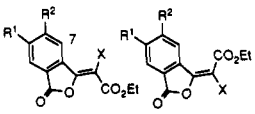
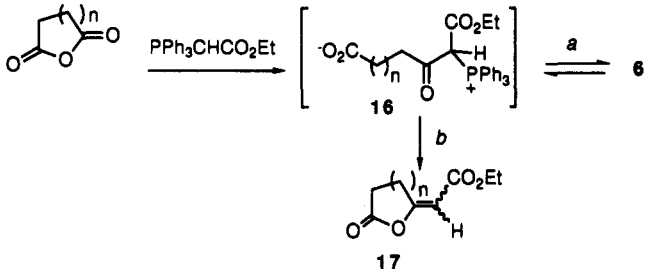
0022-3263/93/1958-1531$04.00/0

Table I. Halogenation of Keto Acid Phosphorane 6: Synthesis of Halo Enol Lactones

substrate	R^1	R^2	electrophile X^+	halo enol lactone yield ($E+Z$ %)[a]	E (%)	Z (%)[b]
						
6a	-	-	Br_2	77	10a(70)	11a(30)
	-	-	SO_2Cl_2	92	10b(86)	11b(14)
						
6b	H	H	Br_2	85	12a(82)	13a(10)[c]
	H	H	SO_2Cl_2	73	12b(96)	13b(4)
6c	Me	Me	Br_2	86	12c(88)	13c(12)
	Me	Me	SO_2Cl_2	70	12d(88)	13d(12)
6d	Me	H	Br_2	91	12e(85)	13e(15)
						
6e	H	H	Br_2	55 (85)[d]	14a(35)	15a(65)
	H	H	SO_2Cl_2	62	14b(44)	15b(56)
6f	Cl	Cl	Br_2	44 (61)[d]	14c(20)	15c(80)
	Cl	Cl	SO_2Cl_2	93	14d(23)	15d(77)

[a] Isolated yield after chromatography. [b] Ratio taken from ^1H NMR spectrum of crude product. [c] 8% endocyclic isomer detected by ^1H NMR spectroscopy. Not isolated. [d] Yield obtained from the reaction of PPh_3CBrCO_2Et with the anhydride.

Scheme III

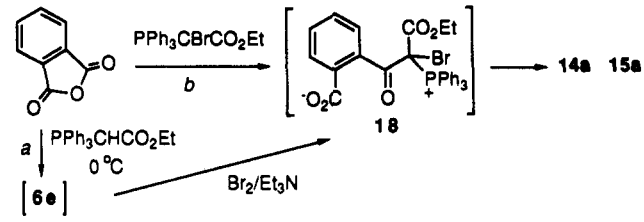


and purified by silica chromatography, and the isomers were separated by HPLC. A similar treatment of **6a** with SO_2Cl_2 and Et_3N, at −78 °C, gave the corresponding five-membered chloro enol lactones **10b** and **11b**. The six-membered bromo enol lactones and chloro enol lactones, **12** and **13**, and the aromatic bromo and chloro enol lactones, **14** and **15**, were also synthesized from the corresponding keto acid phosphoranes (Table I).

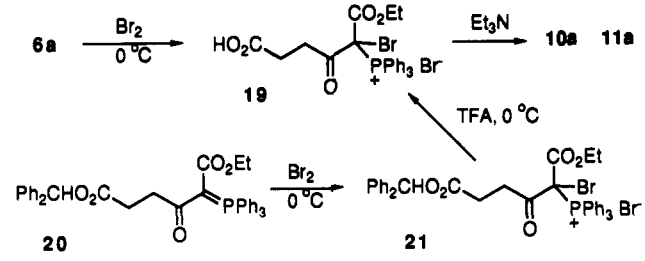
The starting keto acid phosphoranes **6** were conveniently prepared[6] by reaction of a cyclic anhydride with PPh_3CHCO_2Et (Scheme III, pathway a). Prelonged reaction results in the formation of the hydrogen enol lactone **17**, rather than **6**, via cyclization of the intermediate phosphonium salt **16**. Compound **6a** has also been prepared[10] via the reaction of PPh_3CHCO_2Et with benzhydryl succinyl chloride, followed by removal of the benzhydryl protecting group with TFA.

The bromo enol lactones **10–13** could not be prepared by reaction of a cyclic anhydride with PPh_3CBrCO_2Et (Scheme II, pathway b). The bromo ylide is less nucleophilic than PPh_3CHCO_2Et. The phthalic bromo enol lactones **14a** and **15a** were, however, obtained in a similar yield and isomer ratio, via both the bromolactonization of

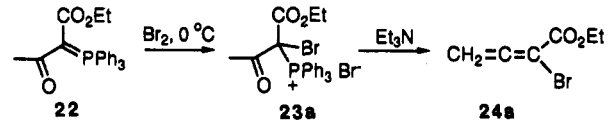
Scheme IV



Scheme V



Scheme VI



6e and the direct reaction of phthalic anhydride with PPh_3CBrCO_2Et (Scheme IV, pathways a and b). A common reaction mechanism is therefore likely, with a different method of producing the key intermediate **18** (or **7** in the general Scheme II). The bromo lactonization reaction (Scheme II, pathways a) avoids the initial slow reaction of PPh_3CBrCO_2Et with the anhydride (Scheme II, pathway b), by forming the desired halo phosphonium salt intermediate **7** via halogenation of the keto acid phosphorane.

The proposed intermediates in the formation of the halo enol lactones **10a** and **11a**, the bromo phosphonium salt **7** (n = 1, X = Br), and the betaine **8** (n = 1, X = Br) (Scheme II), were not detected by ^1H NMR spectroscopy on the bromination of **6a** with Br_2 and Et_3N at −40 °C. However, reaction of **6a**, with Br_2, at 0 °C and in the absence of Et_3N, did yield the bromo phosphonium salt **19** (Scheme V). Treatment of **19** with Et_3N then gave the bromo enol lactones **10a** and **11a** (2:1). Compound **19** was also prepared indirectly, via the bromination of **20**[10] to give **21**, followed by removal of the benzhydryl ester with TFA (Scheme V). The reaction of the keto acid phosphorane **22** with Br_2, at 0 °C, gave the bromo phosphonium salt **23a**. Treatment with Et_3N then gave the bromoallene **24a** (Scheme VI).

The OCH_2CH_3 proton resonances of **19**, **21**, and **23a** were characteristically[11] downfield (ca. 0.5 ppm) relative to acyl phosphoranes such as **6a**, **20**, and **22**. The PPh_3 C-1 resonance of **19** and **23a** was also in a characteristic[11] upfield position with an expected ^{13}C–^{31}P coupling constant of 88 Hz. The C–PPh_3 resonance of **19** and **23a** was also characteristic[11] at δ 62.2 and 62.6, respectively (^{13}C–^{31}P coupling constant of 50 Hz in both cases). Resonances at δ 33 and 38 in the broad band decoupled ^{31}P spectra of **19** and **23a**, respectively, were also consistent[11] with the proposed phosphonium salt structures.

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Scheme VII

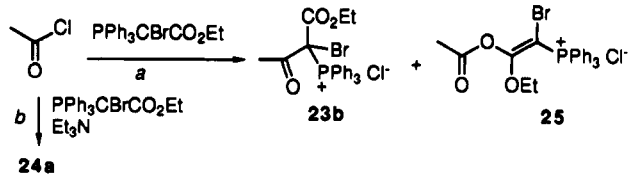
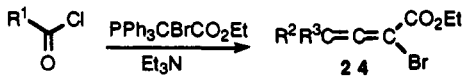
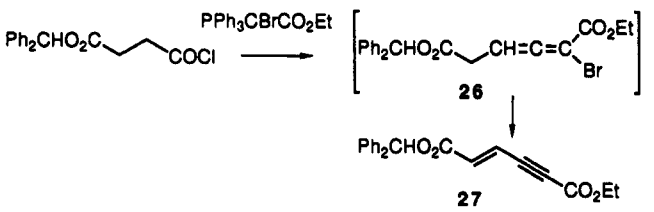


Table II. Preparation of Bromoallenes 24

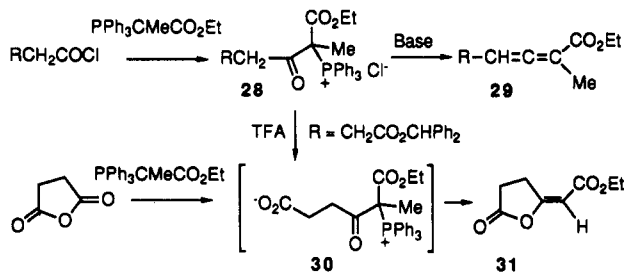


acid chloride R^1	bromoallene	R^2	R^3	yield (%)
Me	**24a**	H	H	88
$CHMe_2$	**24b**	Me	Me	80
CH_2CH_2Me	**24c**	H	CH_2Me	89

Scheme VIII



Scheme IX

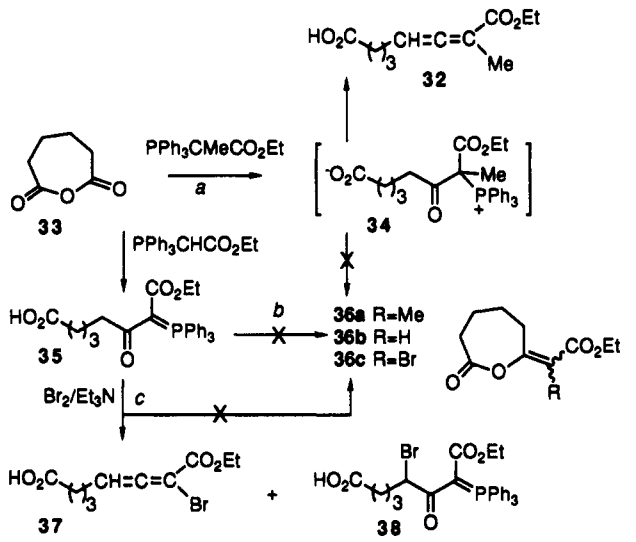


The bromoallene **24a** was also prepared via the reaction of acetyl chloride with PPh_3CBrCO_2Et and Et_3N (Scheme VII, pathway b). Treatment of PPh_3CBrCO_2Et with Et_3N and an acid chloride represents a convenient and general preparation of bromoallenes (Table II).

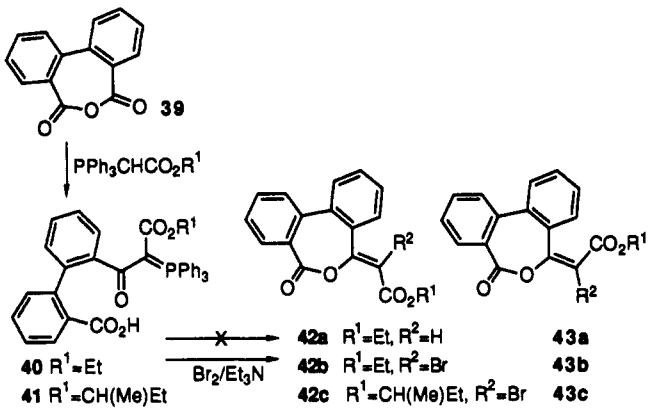
The reaction of acetyl chloride with PPh_3CBrCO_2Et, in the absence of Et_3N, gave a mixture of the expected bromo phosphonium salt **23b** and a compound tentatively assigned, on the basis of ^1H NMR data, as the O-acylated derivative **25** (Scheme VII, pathway a). The reaction of an acid chloride with PPh_3CMeCO_2Et is known to give an analogous *O*-acyl derivative as the initial product.[11] The reaction of (diphenylmethoxy)carbonyl)propionyl chloride with PPh_3CBrCO_2Et gave the vinyl acetylene **27**, presumably formed via the bromoallene **26** (Scheme VIII).

The analogous methyl phosphonium salts **28** are also known[10] to yield the allenes **29** on treatment with base (Scheme IX). Phosphonium salts, of the type **30**, have been postulated[10] as key intermediates in the Wittig reaction between a cyclic anhydride and PPh_3CMeCO_2Et (Scheme IX). Removal of the benzhydryl protecting group from **28** ($R = CH_2CO_2CHPh_2$) did yield the enol lactone **31**, presumably via **30** (Scheme IX). An acyclic intermediate is only observed in the Wittig reaction of a cyclic anhydride with a stabilized ylide when rearrangement of the initially formed phosphonium salt to a stable keto acid phosphorane to possible, as in the conversion of **16** to **6** (Scheme III).

Scheme X



Scheme XI



As opposed to succinic anhydride (Scheme IX), adipic anhydride **33** reacts with PPh_3CMeCO_2Et, via the phosphonium salt **34**, to give the allene **32** rather than the enol lactone **36a** (Scheme X, pathway a).[10] Bromination of the adipic-derived keto acid phosphorane **35** also failed to give the seven-membered bromo enol lactone **36c**, but rather gave the bromoallene **37** and the α-bromo keto acid phosphorane **38**, products of an acyclic pathway (Scheme X, pathway c). The bromoallene **37** failed to give the bromo enol lactone **36c** on extended heating in $CDCl_3$. Hence allenes are unlikely intermediates in the halolactonization reaction. The keto acid phosphorane **40**, derived from diphenic anhydride **39** (Scheme XI), did yield the corresponding bromo enol lactones **42b** and **43b** (37:63), presumably since the alternative allene pathway, taken by **35** (Scheme X, pathway c), is not available. Extended heating of the diphenic keto acid phosphorane **40** in $CDCl_3$, at 60 °C, failed to yield the hydrogen enol lactones **42a** or **43a**. The bromination conditions must, therefore, promote cyclization. The adipic derived keto acid phosphorane **35** also failed to cyclize on heating in $CDCl_3$, at 60 °C, for 60 h (Scheme X, pathway b).

Phosphonium salts of the type **7** (X = H, Me, or Br, Scheme II) can, therefore, react in either of three ways. Cyclization to give an enol lactone (e.g. the formation of **9**, Scheme II). Alternatively, for X = H, migration of a proton can occur to give the keto acid phosphorane **6** (Scheme III). Enolization followed by the loss of triphenylphosphine oxide yields an allene when cyclization

is not favored (due to either a large ring size (Scheme X, pathway a and c) or the absence of a free carboxyl group (Table II and Scheme VI)).

The ease of keto acid phosphorane halolactonization (Scheme II, pathway a), relative to the alternative cyclization to a hydrogen enol lactone (e.g. the formation of **17**, Scheme II), suggests that the halolactonization is unlikely to proceed via initial formation of a hydrogen enol lactone, followed by incipient halogenation. Indeed, treatment of the hydrogen enol lactone **17** (n = 1) under the standard bromolactonization conditions gave a very poor yield of the bromo enol lactones **10a** and **11a**.[3]

The *E*-halo enol lactone was the major isomer in the five- and six-membered series while the *Z* isomer predominated with the phthalic-based examples (Table I). The configuration of the halo enol lactones **10–15** was tentatively assigned by comparison of the ^{1}H NMR spectra of structurally similar enol lactones.[6,13] The ethyl ester in the *Z* configuration is known to deshield $(H3)_2$ in succinic- and glutaric-based enol lactones **11** and **13** and H7 in phthalic based enol lactones **15** (see Table I for numbering scheme). X-ray crystal structures of **11a**, **15a**,[3] and **15c** provided suitable reference configurations. Some ambiguity existed in the phthalic series due to the deshielding effect of bromine. The H7 resonance of the *Z*-halo enol lactones **15b**, **15c**, and **15d** is downfield relative to the corresponding *E* isomers **14b**, **14c**, and **14d** as expected.[6] However, the *Z*-bromo phthalic enol lactone **15a** (configuration confirmed by an X-ray crystal structure) gave a resonance for H7 (δ 8.58) upfield relative to the corresponding *E* isomer **14a** (δ 8.70). The ester carbonyl and the ylidine carbon resonances are consistently downfield in the *Z* isomers **15a**, **15b**, **15c**, and **15d**, relative to the corresponding *E* isomers **14a**, **14b**, **14c**, and **14d**, respectively.

The configuration of the minor isomer **42b**, derived from the bromination of the diphenic derived keto acid phosphorane **40**, was assigned as *E* on the basis of a single-crystal X-ray structure determination. The upfield position of the OCH_2CH_3 resonances of the *Z* isomer **43b** (δ 0.97 and 3.99), relative to the *E* isomer **42b** (δ 1.38 and 4.32), in $CDCl_3$, is consistent with the shielding influence of the aromatic ring and hence the assigned configurations. The OCH_2 resonances appeared as a multiplet in DMSO-d_6 at δ 4.00 and 4.35 for **43b** and **42b**, respectively. Each of these resonances collapsed to a distorted AB quartet on irradiation of the OCH_2CH_3 resonances at δ 0.93 and 1.37, respectively. Inversion of the biphenyl group must, therefore, be slow on the NMR time scale at 25 °C.

Treatment of the keto acid phosphorane **41**[14] with Br_2 and Et_3N gave four products, a pair of biphenyl conformations for each of the *E*- and *Z*-bromo enol lactones **42c** and **43c** (29:71), respectively. Radial chromatography gave pure *Z*-bromo enol lactones **43c** as a conformational pair and a second fraction containing all four isomers. The *Z*-bromo enol lactones **43c** exhibited a characteristic upfield shift for the ester protons, as discussed for **43b**. In the ^{13}C NMR spectrum of **43c** twined signals were observed, confirming the presence of two diastereoisomers. The ^{13}C NMR spectrum of the mixture of all four diastereoisomers of **42c** and **43c** was complex, but the resonances for the ester group clearly indicated the presence of all four diastereoisomers.

The barrier to interconversion of the biphenyl conformers of the *Z*-bromo enol lactone **43b** in DMSO-d_6 (300 MHz), measured from the coalescence (T_c = 67 °C) of the OCH_2 multiplet at δ 4.00 (AB q with irradiation at δ 0.95, J = 11.1 Hz) to a broad quartet, J = 7.1 Hz (singlet with irradiation at δ 0.95) was determined[15] to be $\Delta G^{\ddagger}$ 20 kcal mol^{-1}. A similar analysis on the *E*-bromo enol lactone **42b** (T_c = 80 °C) gave a $\Delta G^{\ddagger}$ value of 21 kcal mol^{-1}. These values compare favorably to $\Delta G^{\ddagger}$ values calculated for related biphenyls.[16]

Experimental Section

General Methods. Melting points were obtained using a hot stage microscope and are uncorrected. NMR spectra were obtained at 300 MHz for ^{1}H, 75 MHz for ^{13}C, and 122 MHz for ^{31}P. Infrared spectra were obtained using either a Pye Unicam SP3-300 or a Perkin-Elmer 1600 FTIR spectrophotometer. Mass spectra were obtained on a Kratos MS80RFA magnetic sector double-focusing mass spectrometer. Semipreparative HPLC was carried out on a Varian Model 5000 liquid chromatograph, using a Roedyne 7125 injector and a Varian UV-50 ultraviolet detector, with an output to a Hewlett-Packard 3390 A integrator. Preparative chromatography was carried out using a Chromatotron (Harrison Research Inc.) using glass plates coated with silica gel (P.F. 254 60) of 2-mm thickness. All chemicals were reagent grade unless otherwise stated.

General Procedure for the Bromination of the Keto Acid Phosphoranes 6a–f, 35, 40, and 41. A solution of the keto acid phosphorane (typical 0.45 mmol), in CH_2Cl_2 (10 mL), was cooled to 0 °C (−78 °C for **40**). Et_3N (1.1 equiv) followed by Br_2 (1.1 equiv) was added. The solution was stirred under a N_2 atmosphere for 30 min, at 0 °C (−78 °C for **40**) and then allowed to warm to 20 °C. Evaporation under reduced pressure gave the crude bromo enol lactones. An ^{1}H NMR spectrum of the crude mixture allowed an estimation of the *E* and *Z* isomer ratio. The products were purified by chromatography, on a 2-mm silica chromatotron plate.

(a) Bromo Enol Lactones 10a and 11a (Isomer Ratio 70:30 by ^{1}H NMR). Elution with CH_2Cl_2 gave a mixture of the *E*- and *Z*-bromo enol lactones **10a** and **11a** as an oil (77%). The isomers were separated by HPLC, using a 10-mm Econosphere CN column, with a UV spectrographic detector at 256 nm, eluting with CH_2Cl_2/petroleum ether (25:70), with a flow rate of 4 mL min^{-1}. Ethyl (*E*)-bromo(5-oxotetrahydrofuran-2-ylidene)acetate (**10a**) was recrystallized from benzene as white plates: mp 148–149 °C; IR (Nujol) 1833, 1713, 1639; ^{1}H NMR ($CDCl_3$) δ 1.36 (t, J = 7.0 Hz, OCH_2OH_3), 2.78 (m, $(H4)_2$), 3.10 (m, $(H3)_2$), 4.31 (q, J = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.1, 26.0, 27.9, 62.3, 93.9, 158.9, 161.1, 173.4; HRMS calcd for $C_8H_9{}^{79}BrO_4$ 247.9685, found 247.9683. Ethyl (*Z*)-bromo(5-oxotetrahydrofuran-2-ylidene)acetate (**11a**) was recrystallized from benzene to give flat needles: mp 154–156 °C; IR (Nujol) 1826, 1692, 1638; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.0 Hz, OCH_2CH_3), 2.85 (m, $(H4)_2$), 3.41 (m, $(H3)_2$), 4.28 (t, J = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.1, 26.9, 29.1, 62.0, 89.6, 162.9, 163.5, 172.2; HRMS calcd for $C_8H_9{}^{79}BrO_4$ 247.9685, found 247.9682.

(b) Bromo Enol Lactones 12a and 13a (Isomer Ratio 82:10:8 Endocyclic Isomer by ^{1}H NMR). Elution with CH_2Cl_2 gave ethyl (*E*)-bromo(6-oxotetrahydropyran-2-ylidene)acetate (**12a**) as a clear oil (76%): IR (Nujol) 1714; ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J = 7.0 Hz, OCH_2CH_3), 1.97 (m, $(H4)_2$), 2.67 (t, J = 6.5 Hz, $(H5)_2$), 2.80 (t, J = 6.5 Hz, $(H3)_2$), 4.29 (q, J = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.0, 17.3, 27.2, 29.9, 62.3, 98.0, 155.2, 162.1, 165.4; HRMS calcd for $C_9H_{11}{}^{79}BrO_4$ 261.9841, found 261.9845. Ethyl (*Z*)-bromo(6-oxotetrahydropyran-2-ylidene)acetate (**13a**) was obtained as an oil (9%): IR (Nujol) 1714; ^{1}H NMR ($CDCl_3$)

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δ 1.35 (t, J = 7.0 Hz, OCH_2CH_3), 1.95 (m, $(H4)_2$), 2.71 (t, J = 6.4 Hz, $(H5)_2$), 3.15 (t, J = 6.4 Hz, $(H3)_2$), 4.27 (q, J = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 13.9, 17.7, 27.6, 30.6, 62.2, 95.0, 161.0, 163.2, 165.5; HRMS calcd for $C_9H_{11}{}^{79}BrO_4$ 261.9841, found 261.9827. The endocyclic isomer was observed in the crude mixture, by ^1H NMR spectroscopy, but was not isolated: ^1H NMR ($CDCl_3$) δ 1.36 (t, J = 7.0 Hz, OCH_2CH_3), 1.95 (m, $(H5)_2$), 2.44 (m, $(H4)_2$), 4.30 (q, J = 7.0 Hz, OCH_2CH_3), 5.72 (t, J = 5.0 Hz, H3), 5.89 (s, CHBr).

(c) Bromo Enol Lactones 12c and 13c (Isomer Ratio 88:12 by ^1H NMR). Elution with CH_2Cl_2 gave ethyl (*E*)-bromo(4,4-dimethyl-6-oxotetrahydropyran-2-ylidene)acetate (**12c**) as a clear oil (77%): IR (Nujol) 1781, 1720, 1607; ^1H NMR ($CDCl_3$) δ 1.12 (s, 2 × Me), 1.34 (t, J = 7.1 Hz, OCH_2CH_3), 2.47 (s, $(H5)_2$), 2.65 (s, $(H3)_2$), 4.30 (q, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 13.8, 27.6, 29.7, 40.3, 43.1, 61.9, 98.0, 154.1, 161.9, 165.0; HRMS calcd for $C_{11}H_{15}{}^{79}BrO_4$ 290.0154, found 290.0159. Ethyl (*Z*)-bromo(4,4-dimethyl-6-oxotetrahydropyran-2-ylidene)acetate (**13c**) was obtained as a clear oil (9%): IR (Nujol) 1784, 1704, 1605; ^1H NMR ($CDCl_3$) δ 1.10 (s, 2 × Me), 1.36 (t, J = 7.1 Hz, OCH_2CH_3), 2.53 (s, $(H5)_2$), 3.01 (s, $(H3)_2$), 4.29 (q, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.1, 27.7, 29.7, 39.7, 44.2, 62.3, 95.6 159.7, 163.6, 166.1; HRMS calcd for $C_{11}H_{15}{}^{79}BrO_4$ 290.0154, found 290.0176.

(d) Bromo Enol Lactones 12e and 13e (Isomer Ratio 85:15 by ^1H NMR). Elution with CH_2Cl_2 gave ethyl (*E*)-bromo(4-methyl-6-oxotetrahydropyran-2-ylidene)acetate (**12e**) as a clear oil (77%): ^1H NMR ($CDCl_3$) δ 1.12 (d, J = 6.1 Hz, $CHCH_3$), 1.32 (t, J = 7.0 Hz, OCH_2CH_3), 2.30 (m, $H5_a$, $H3_a$ and H4), 2.70 (dd, J = 2.6, 15.5 Hz, $H5_b$), 3.05 (dd, J = 2.6, 15.5 Hz, $H3_b$), 4.28 (q, J = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.0, 20.5, 24.9, 35.1, 37.6, 62.4, 98.1, 154.5, 162.2, 165.3; HRMS calcd for $C_{10}H_{13}BrO_4$ 275.9997, found 276.0058. Ethyl (*Z*)-bromo(4-methyl-6-oxotetrahydropyran-2-ylidene)acetate (**13e**) was obtained as a clear oil (14%): ^1H NMR ($CDCl_3$) δ 1.12 (d, J = 6.0 Hz, $CHCH_3$), 1.35 (t, J = 7.0 Hz, OCH_2CH_3), 2.17 (m, H4), 2.33 (dd, J = 10.4, 17.2 Hz, $H5_a$), 2.53 (dd, J = 10.4, 17.4 Hz, $H3_a$), 2.79 (dd, J = 1.9, 17.2 Hz, $H5_b$), 3.53 (ddd, J = 1.9, 4.3, 17.2 Hz, $H3_b$), 4.27 (t, J = 7.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.1, 20.4, 25.2, 34.3, 38.3, 62.3, 95.2, 160.0, 163.6, 165.4.

(e) Bromination of Phosphorane 35.[10] Elution with ethyl acetate/petroleum ether (2:3) gave the bromo allene **37**, as an unstable oil, which was not purified further (23%): ^1H NMR ($CDCl_3$) δ 1.31, (t, J = 7.1 Hz, OCH_2CH_3), 1.87 (m, CH_2), 2.33 (q, J = 7.1 Hz, CH_2), 2.47 (dt, J = 1.4, 7.2 Hz, CH_2), 4.27 (q, J = 7.2 Hz, OCH_2CH_3), 5.70 (t, J = 6.9 Hz, CH); ^{13}C NMR ($CDCl_3$) δ 14.1, 23.0, 27.0, 32.7, 62.9, 84.5, 100.3, 140.3, 178.5, 208.2; HRMS calcd for $C_{10}H_{14}{}^{79}BrO_4$ 277.0076, found 277.0077. Further elution gave the α-bromo phosphorane **38** as an unstable oil (34%): ^1H NMR δ ($CDCl_3$) 0.65 (t, J = 7.2 Hz, OCH_2CH_3), 1.60–2.10 (m, 4 H), 2.28 (t, J = 7.6 Hz, CH_2CO_2H), 3.73 (dq, J = 1.0, 7.1 Hz, OCH_2CH_3), 5.94 (t, J = 7.2 Hz, CHBr), 7.20–7.70 (m, arom); ^{13}C NMR ($CDCl_3$) δ 13.6, 22.8, 33.4, 33.6, 50.6, (d, J = 7.7 Hz), 58.8, 70.5 (d, J = 108.9 Hz), 125.9 (d, J = 93.8 Hz), 128.6 (d, J = 12.7 Hz), 131.8 (d, J = 3.0 Hz) 133.0 (d, J = 9.9 Hz), 167.1 (d, J = 13.6 Hz), 178.2, 190.2 (d, J = 4.4 Hz); HRMS (FAB) calcd for $C_{28}H_{29}{}^{79}BrO_5P$ 555.0936, found 555.0938.

(f) Bromo Enol Lactones 42b and 43b (Isomer Ratio 37:63 by ^1H NMR). Elution with ethyl acetate/petroleum ether (2:3) gave a mixture of the *E*- and *Z*-bromo enol lactones **42b** and **43b** as an oil (83%). Crystallization from ethyl acetate/petroleum ether gave ethyl (*E*)-bromo(5,7-dihydro-7-oxodibenz[*c*,*e*]oxepin-5-ylidine)acetate (**42b**) as colorless crystals (10%): mp 179.5–180.5 °C; ^1H NMR ($CDCl_3$) δ 1.38 (t, J = 7.2 Hz, OCH_2CH_3), 4.32 (m, OCH_2CH_3), 7.48–8.00 (m, 8 H, arom); ^{13}C NMR ($CDCl_3$) δ 13.9, 63.0, 106.7, 128.8, 129.1, 129.8, 129.9, 130.1, 130.9, 131.1, 131.2, 134.0, 136.2, 137.1, 137.4, 151.5, 162.0, 165.2. Anal. Calcd for $C_{18}H_{13}BrO_4$: C, 57.93; H, 3.51. Found: C, 58.18; H, 3.56. The *Z* isomer **43b** (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 0.97 (t, J = 7.2 Hz, OCH_2CH_3), 3.99 (q, J = 7.2 Hz, OCH_2CH_3), 7.44–7.99 (m, 8 H, arom); ^{13}C NMR ($CDCl_3$) δ 13.4, 62.4, 106.5, 128.2, 128.4, 128.6, 128.9, 129.1, 130.9, 131.9, 132.1, 133.3, 133.4, 155.1, 162.1, 164.6.

(g) Bromo Enol Lactones 42c and 43c (Isomer Ratio 29:71 by ^1H NMR). Elution with CH_2Cl_2/petroleum ether (4:1) gave a fraction containing a mixture of the *E*- and *Z*- bromo enol lactones **42c** and **43c** (43%) and pure fraction of 2-butyl (*Z*)-bromo(5,7-dihydro-7-oxodibenz[*c*,*e*]oxepin-5-ylidine)acetate (**43c**) as a white solid (10%): mp 77–80 °C; IR (KBr) 1761, 1640; ^1H NMR ($CDCl_3$) δ 0.60, 0.66 (2 t, J = 7.5, 7.4 Hz, CH_2CH_3), 0.90, 1.00 (2 d, J = 6.3, 6.4 Hz, $CHCH_3$), 1.18–1.38 (bm, CH_2CH_3), 4.97 (m, OCH), 7.41–7.96 (m, arom); ^{13}C NMR ($CDCl_3$) δ 9.1, 9.2, 18.6, 18.7, 28.1, 28.3, 75.0, 75.1, 106.9, 107.5, 128.2, 128.4, 128.5, 128.7, 129.0, 129.1, 130.9, 131.0, 154.2, 154.8, 161.8, 161.9, 164.7, 164.8. Anal. Calcd for $C_{20}H_{17}BrO_4$: C, 59.86; H, 4.27. Found: C, 59.62; H, 4.22. Minor *E* isomer **42c** (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 0.92, 0.97 (2 t, J = 7.4, 7.5 Hz, CH_2CH_3), 1.26, 1.34 (2 d, J = 6.2, 6.3 Hz, $CHCH_3$), 1.18–1.38 (bm, CH_2CH_3), 5.00 (m, OCH), 7.41–7.71 (m, arom); ^{13}C NMR ($CDCl_3$) δ 9.6, 9.7, 19.1, 19.3, 28.6, 28.7, 75.7, 75.8, 108.0 (no other signals were able to be assigned due to extensive overlap).

General Procedure for the Preparation of Bromo Enol Lactones 14a, 14c, 15a and 15c: Method A. PPh_3CBrCO_2Et (1.1 equiv) was added to a stirred solution of phthalic anhydride or 4,5-dichlorophthalic anhydride (typically 0.68 mmol), in $CHCl_3$ (10 mL), at 25 °C. After 2 h at reflux (phthalic anhydride), or 5 h at 20 °C (4,5-dichlorophthalic anhydride), the solvent was removed under reduced pressure. An ^1H NMR spectrum, of the crude mixture, allowed estimation of the *E* and *Z* isomer ratio. The products were purified by chromatography, on a 2-mm silica chromatotron plate.

(a) Bromo Enol Lactones 14a and 15a (Isomer Ratio 35:65 by ^1H NMR). Elution with a gradient of CH_2Cl_2 in petroleum ether gave a fraction containing a mixture of **14a** and **15a** (74%). A second fraction contained ethyl (*Z*)-bromo(3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**15a**) crystallized from ethyl acetate/petroleum ether as striated needles (11%): mp 214–215 °C; IR (Nujol) 1785, 1741, 1711; ^1H NMR ($CDCl_3$) δ 1.43 (t, J = 7.1 Hz, OCH_2CH_3), 4.42 (q, J = 7.1 Hz, OCH_2CH_3), 7.67 (t, J = 8.0 Hz, H6), 7.78 (t, J = 8.0 Hz, H5), 7.95 (d, J = 8.0 Hz, H4), 8.58 (d, J = 8.0 Hz, H7); ^{13}C NMR ($CDCl_3$) δ 14.1, 63.0, 97.0, 125.9, 126.4, 126.8, 132.0, 135.4, 153.7, 163.1, 164.5; HRMS calcd for $C_{12}H_9{}^{79}BrO_4$ 295.9685, found 295.9685. Ethyl (*E*)-bromo(3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**14a**) (data obtained from mixture): ^1H NMR δ ($CDCl_3$) 1.42 (t, J = 7.1 Hz, OCH_2CH_3), 4.42 (q, J = 7.1 Hz, OCH_2CH_3), 7.75 (t, J = 8.0 Hz, H6), 7.82 (t, J = 8.0 Hz, H5), 8.00 (d, J = 8.0 Hz, H4), 8.70 (d, J = 8.0 Hz, H7); ^{13}C NMR ($CDCl_3$) δ 14.1, 63.1, 97.0, 126.2, 126.4, 131.3, 132.3, 135.0, 137.7, 149.5, 162.7, 164.7.

(b) Bromo Enol Lactones 14c and 15c (Isomer Ratio 20:80 by ^1H NMR). Elution with CH_2Cl_2/petroleum ether (50:50) gave ethyl (*Z*)-bromo(5,6-dichloro-3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**15c**) as a white solid, which was recrystallized from petroleum ether (47%): mp 165–166 °C; ^1H NMR ($CDCl_3$) δ 1.44 (t, J = 7.1 Hz, OCH_2CH_3), 4.43 (q, J = 7.1 Hz, OCH_2CH_3), 8.02 (s, H4), 8.86 (s, H7); ^{13}C NMR ($CDCl_3$) δ 14.1, 63.3, 99.0, 125.9, 127.2, 128.3, 129.1, 137.2, 140.7, 152.4, 162.4, 162.7. Anal. Calcd for $C_{12}H_7Cl_2BrO_4$: C, 39.4; H, 1.9. Found: C, 39.4; H, 1.9. Further elution gave ethyl (*E*)-bromo(5,6-dichloro-3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**14c**) as a white solid, which was recrystallized from petroleum ether (14%): mp 154–155 °C; IR (KBr) 1810, 1720, 1620; ^1H NMR δ ($CDCl_3$) 1.41 (t, J = 7.1 Hz, OCH_2CH_3), 4.42 (q, J = 7.1 Hz, OCH_2CH_3), 8.08 (s, H4), 8.77 (s, H7); ^{13}C NMR ($CDCl_3$) δ 14.1, 63.3, 98.7, 125.5, 127.6, 127.9, 136.2, 137.5, 140.2, 147.7, 161.3, 162.4; HRMS (CI) calcd for $C_{12}H_8{}^{79}Br^{35}Cl_2O_4$ 364.8983, found 364.8980.

Method B. PPh_3CHCO_2Et (1 equiv) and phthalic anhydride or 4,5-dichlorophthalic anhydride (typically 0.67 mmol) were stirred in $CHCl_3$ (10 mL) at 0 °C for 30 min (phthalic anhydride) or at 20 °C for 10 min (4,5-dichlorophthalic anhydride). Et_3N (0.7 equiv), followed by Br_2 (0.7 equiv), was added, and the solution was stirred for a further 30 min at the given temperature. The solvent was removed under reduced pressure. An ^1H NMR spectrum of the crude mixture gave the ratio of *E* and *Z* isomers. The bromo enol lactones were purified by chromatography on a 2-mm silica chromatotron plate.

(a) Bromo Enol Lactones 14a and 15a (Isomer Ratio 35:65 by ^1H NMR). Elution with CH_2Cl_2 gave a white solid containing a mixture of the *E*- and *Z*-bromo enol lactones **14a** and **15a** (55%). Spectral data were identical to that given above.

(b) Bromo Enol Lactones 14c and 15c (Isomer Ratio 20:80 by ^1H NMR). Elution with CH_2Cl_2/petroleum ether (50:50) gave

the *E*-bromo enol lactones **14c** (8%) and the *Z*-bromo enol lactone **15c** (36%). Spectral data was identical to that given above.

General Procedure for the Calculation of the Keto Acid Phosphoranes 6a–c. A solution of the keto acid phosphorane (typical 0.8 mmol), in CH_2Cl_2 (20 mL), was cooled to −78 °C, and SO_2Cl_2 (1.5 equiv), followed by Et_3N (1.5 equiv), was added. The solution was stirred at −78 °C, under a N_2 atmosphere, for 30 min and then allowed to warm to 20 °C. Evaporation under reduced pressure gave the crude bromo enol lactones. An ^1H NMR spectrum, of the crude mixture, allowed estimation of the *E* and *Z* isomer ratio. The products were purified by chromatography on a 2-mm silica chromatotron plate.

(a) Chloro Enol Lactones 10b and 11b (Isomer Ratio 86:14 by ^1H NMR). Elution with ethyl acetate/petroleum ether (45:55) gave an inseparable mixture of the *E*- and *Z*-bromo enol lactones **10b** and **11b** as an oil (92%): IR (Nujol) 1840, 1720, 1650. Anal. Calcd for $C_8H_9ClO_4$: C, 46.96; H, 4.43; Cl, 17.33. Found: C, 46.36; H, 4.32; Cl, 17.30. Ethyl (*E*)-chloro(5-oxotetrahydrofuran-2-ylidene)acetate (**10b**) (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 1.35 (t, J = 7.2 Hz, OCH_2CH_3), 2.78 (m, $(H4)_2$, 3.14 (m, $(H3)_2$), 4.32 (q, J = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.0, 25.5, 27.1, 62.0, 104.1, 158.5, 160.9, 173.3. Ethyl (*Z*)-chloro(5-oxotetrahydrofuran-2-ylidene)acetate (**11b**) (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 1.36 (t, J = 7.1 Hz, OCH_2CH_3), 2.83 (m, $(H4)_2$), 3.43 (m, $(H3)_2$), 4.30 (q, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.0, 26.5, 27.3, 61.9, 101.4, 161.6, 162.9, 172.3.

(b) Chloro Enol Lactones 12b and 13b (isomer ratio 96:4 by ^1H NMR). Elution with ethyl acetate/petroleum ether (15:85) gave an inseparable mixture of the *E*- and *Z*-bromo enol lactones **12b** and **13b** as an oil (73%): IR (Nujol) 1790, 1720, 1620; HRMS calcd for $C_9H_{11}{}^{35}ClO_4$ 218.0346, found 218.0348. Ethyl (*E*)-chloro-(6-oxotetrahydropyran-2-ylidene)acetate (**12b**) (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 1.35 (t, J = 7.1 Hz, OCH_2CH_3), 2.00 (quin, J = 6.7 Hz, $(H4)_2$), 2.65 (t, J = 6.7 Hz, $(H5)_2$), 2.83 (t, J = 6.7 Hz, $(H3)_2$), 4.31 (q, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.1, 17.2, 25.5, 30.1, 62.2, 108.6, 155.4, 161.6, 165.4. Ethyl (*Z*)-chloro-(6-oxotetrahydropyran-2-ylidene)acetate (**13b**) (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 1.35 (t, J = 7.2 Hz, OCH_2CH_3), 1.97 (quin, J = 6.6 Hz, $(H4)_2$), 2.72 (t, J = 6.6 Hz, $(H5)_2$), 3.20 (t, J = 6.6 Hz, $(H3)_2$), 4.28 (q, J = 7.2 Hz, OCH_2CH_3).

(c) Chloro Enol Lactones 12d and 13d (Isomer Ratio 88:12 by ^1H NMR). Elution with ethyl acetate/petroleum ether (35:65) gave an inseparable mixture of the *E*- and *Z*-bromo enol lactones **12d** and **13d** as an oil (70%): HRMS calcd for $C_{11}H_{15}{}^{35}ClO_4$ 246.0660, found 246.0659. Ethyl (*E*)-chloro(4,4-dimethyl-6-oxotetrahydropyran-2-ylidene)acetate (**12d**) (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 1.13 (s, 2 Me), 1.35 (t, J = 7.1 Hz, OCH_2CH_3), 2.49 (m, $(H5)_2$), 2.66 (m, $(H3)_2$), 4.32 (q, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.1, 28.0, 29.7, 39.0, 43.5, 62.1, 108.9, 154.6, 161.6, 165.1. Ethyl (*Z*)-chloro(4,4-dimethyl-6-oxotetrahydropyan-2-ylidene acetate (**13d**) (data obtained from mixture): ^1H NMR ($CDCl_3$) δ 1.10 (s, 2 Me), 1.36 (t, J = 7.1 Hz, OCH_2CH_3), 2.54 (m, $(H5)_2$), 3.05 (m, $(H3)_2$), 4.28 (q, J = 7.1 Hz, OCH_2CH_3).

General Procedure for the Preparation of Chloro Enol Lactones 14b, 14d, 15b, and 15d. PPh_3CHCO_2Et (1.1 equiv) was added to a stirred solution of phthalic anhydride or 4,5-dichlorophthalic anhydride (typically 0.47 mmol) in $CHCl_3$ (8 mL), at 0 °C. After 15 min SO_2Cl_2 (1.5 equiv), followed by Et_3N (1.5 equiv), was added, and the solution was stirred for 1 h at 0 °C. The solvent was removed under reduced pressure. An ^1H NMR spectrum, of the crude mixture, allowed estimation of the *E* and *Z* isomer ratio. The products were purified by chromatography on a 2-mm silica chromatotron plate.

(a) Chloro Enol Lactones 14b and 15b (Isomer Ratio 44:56 by ^1H NMR). Elution with CH_2Cl_2/petroleum ether (44:56) gave ethyl (*Z*)-chloro(3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**15b**) as a white solid, which was recrystallized from petroleum ether (35%): mp 114–115 °C; IR (KBr) 1800, 1720, 1620, 1590; ^1H NMR ($CDCl_3$) δ 1.44 (t, J = 7.1 Hz, OCH_2CH_3), 4.43 (q, J = 7.1 Hz, OCH_2CH_3), 7.68 (dt, J = 1.0, 7.5 Hz, H6), 7.80 (dt, J = 1.3, 8.1 Hz, H5), 7.99 (td, J = 1.0, 7.5 Hz, H4), 8.72 (td, J = 0.8, 8.1 Hz, H7); ^{13}C NMR ($CDCl_3$) δ 14.1, 62.8, 108.1, 125.9, 126.2, 127.2, 132.1, 135.4, 135.7, 152.9, 162.7, 164.4. Anal. Calcd for $C_{12}H_9ClO_4$: C, 57.05; H, 3.59; Cl, 14.03. Found: C, 56.90; H, 3.50; Cl, 14.52. Further elution gave ethyl (*E*)-chloro(3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**14b**), which was recrystallized from petroleum ether (27%): mp 137–139 °C; IR (KBr) 1790, 1720, 1630; ^1H NMR δ ($CDCl_3$) 1.43 (t, J = 7.1 Hz, OCH_2CH_3), 4.43 (q, J = 7.1 Hz, OCH_2CH_3), 7.73 (dt, J = 1.0, 7.5 Hz, H6), 7.85 (dt, J = 1.3, 7.7 Hz, H5), 8.04 (td, J = 1.0, 7.6 Hz, H4), 8.49 (td, J = 0.8, 8.0 Hz, H7); ^{13}C NMR ($CDCl_3$) δ 14.2, 62.9, 108.3, 125.7, 126.2, 126.7, 132.3, 135.2, 137.5, 149.7, 161.5, 164.8. Anal. Calcd for $C_{12}H_9ClO_4$: C, 57.05; H, 3.59; Cl, 14.03. Found: C, 56.90; H, 3.51; Cl, 14.32.

(b) Chloro Enol Lactones 14d and 15d (Isomer Ratio 23:77 by ^1H NMR). Elution with CH_2Cl_2/petroleum ether (60:40) gave ethyl (*Z*)-chloro(5,6-dichloro-3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**15d**), which was recrystallized from petroleum ether (72%): mp 147–149 °C; IR (KBr) 1810, 1720, 1620; ^1H NMR ($CDCl_3$) δ 1.44 (t, J = 7.1 Hz, OCH_2CH_3), 4.44 (q, J = 7.1 Hz, OCH_2CH_3), 8.04 (s, H4), 8.96 (s, H7); ^{13}C NMR ($CDCl_3$) δ 14.0, 63.2, 109.7, 125.5, 127.1, 129.3, 134.5, 137.2, 140.6, 151.4, 162.3, 162.4. Anal. Calcd for $C_{12}H_7Cl_3O_4$: C, 44.82; H, 2.19; Cl, 33.08. Found: C, 44.75; H, 2.05; Cl, 33.30 Further elution gave ethyl (*E*)-chloro(3-oxo-1,3-dihydroisobenzofuran-1-ylidene)acetate (**14d**), which was recrystallized from petroleum ether (21%): mp 171–173 °C; IR (KBr) 1800, 1720, 1630; ^1H NMR δ ($CDCl_3$) 1.42 (t, J = 7.1 Hz, OCH_2CH_3), 4.43 (q, J = 7.1 Hz, OCH_2CH_3), 8.09 (s, H4), 8.58 (s, H7); ^{13}C NMR ($CDCl_3$) δ 14.1, 63.2, 109.7, 125.1, 127.6, 128.1, 136.3, 137.6, 140.5, 147.8, 160.9, 162.6. Anal. Calcd for $C_{12}H_7Cl_3O_4$: C, 44.82; H, 2.19; Cl, 33.08. Found: C, 44.53; H, 1.98; Cl, 33.68.

Bromo Phosphonium Salt 19: Method A. A solution of the keto acid phosphorane **6a** (50 mg, 0.11 mmol), in $CDCl_3$ (0.4 mL), was cooled to 0 °C. Br_2 (1.0 equiv) was added, and the solution was allowed to warm to 20 °C. Bromo phosphonium salt **19**: ^1H NMR δ ($CDCl_3$) 1.09 (t, J = 7.0 Hz, OCH_2CH_3), 2.71 (br, CH_2), 3.31 (m, 1 H), 3.40 (m, 1 H), 4.22 (br q, J = 7.0 Hz, OCH_2CH_3), 7.45–7.90 (m, arom); ^{13}C NMR ($CDCl_3$) δ 13.4, 28.4, 34.8, 62.2 (d, J = 50 Hz), 66.9, 116.7 (br d, J = 88 Hz), 128.8 (d, J = 12 Hz), 132 (d, J = 10 Hz), 133.0, 162.3, 174.6, 196.7; ^{31}P NMR ($CDCl_3$) δ 33 (br). The addition of Et_3N (2 equiv) gave the bromo enol lactones **10a** and **11a** (2:1 by ^1H NMR spectroscopy), which were not purified further.

Method B. A solution of the keto ester phosphorane **20**[10] (10 mg, 0.02 mmol), in $CDCl_3$ (0.4 mL), was cooled to 0 °C. Br_2 (1.0 equiv) was added, and the solution was allowed to warm to 20 °C. Bromo phosphonium salt **21**: ^1H NMR δ ($CDCl_3$) 1.02 (t, J = 7.2 Hz, OCH_2CH_3), 2.78 (br t, J = 6.0 Hz, CH_2), 3.40 (m, 1 H), 3.40 (br t, J = 6.0 Hz, CH_2), 4.22 (br q, J = 7.2 Hz, OCH_2CH_3), 6.80 (s, $CHPh_2$), 7.31 (m, $CHPh_2$), 7.65–7.85 (m, PPh_3). The solution was again cooled to 0 °C, TFA (0.1 mL) was added, and the solution was allowed to warm to 20 °C. Bromo phosphonium salt **19**: ^1H NMR spectral data as above but with superior resolution. $CHCl_3$ (5 mL) was added, and the solution was washed with H_2O (3 × 2 mL). The organic phase was dried and evaporated to give the bromo enol lactones **10a** and **11a** (3:2 by ^1H NMR spectroscopy).

Bromo Phosphonium Salt 23a. A solution of the keto phosphorane **22**[17] (80 mg, 0.21 mmol), in $CDCl_3$ (0.4 mL), was cooled to 0 °C, and Br_2 (1.0 equiv) was added to give the bromo phosphonium salt **23a**: ^1H NMR δ ($CDCl_3$) 1.06 (t, J = 7.0 Hz, OCH_2CH_3), 2.67 (s, Me), 4.17 (q, J = 7.0 Hz, OCH_2CH_3), 7.70–7.90 (m, arom); ^{13}C NMR ($CDCl_3$) δ 13.2, 27.9, 62.6 (d, J = 50 Hz), 66.4, 116.6 (bd, J = 88 Hz), 130.2 (d, J = 13.1 Hz), 134.7 (br), 135.6, 162.5, 195.1; ^{31}P NMR ($CDCl_3$) δ 38. Evaporation gave an unstable, yellow oil: HRMS (FAB) calcd for $C_{22}H_{21}{}^{79}BrO_2P$ (M − C_2H_2O) 427.04630, found 427.04610. The addition of Et_3N (2 equiv) gave the bromoallene **24a** (^1H NMR spectral data as given below), which was not purified further.

General Procedure for the Preparation of Bromoallenes 24a–c. To an ice-cooled, stirred solution of PPh_3CBrCO_2Et (0.23 mmol) in CH_2Cl_2 (5 mL) was added Et_3N (0.23 mmol), followed by the acid chloride (0.23 mmol). After 30 min, the solution was allowed to warm to 20 °C, and the solvent was removed under reduced pressure. Purification by chromatography on a 2-mm

(17) Abell, A. D.; Clark, B. M.; Robinson, W. T. *Aust. J. Chem.* **1989**, *42*, 1161.

silica chromatotron plate, eluting with CH_2Cl_2/ethyl acetate (90:10), gave the bromoallene as an oil which was not purified further (contained traces of triphenylphosphine oxide).

(a) Bromoallene 24a. Yield after chromatography 88%: IR (film) 2983, 1960, 1720; ^1H NMR δ ($CDCl_3$) 1.31 (t, J = 7.2 Hz, OCH_2CH_3), 4.28 (q, J = 7.2 Hz, OCH_2CH_3), 5.31 (s, $=CH_2$); ^{13}C NMR ($CDCl_3$) δ 14.1, 62.9, 84.1, 118.6, 161.7, 211.8; HRMS calcd for $C_6H_7{}^{79}BrO_2$ 189.9630, found 189.9628.

(b) Bromoallene 24b. Yield after chromatography 80%: IR (film) 2979, 1967, 1740; ^1H NMR δ ($CDCl_3$) 1.27 (t, J = 7.1 Hz, OCH_2CH_3), 1.90 (s, 2 Me), 4.24 (q, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 14.2, 19.6, 62.9, 81.3, 107.8, 162.4, 205.9.

(c) Bromoallene 24c. Yield after chromatography 89%: IR (film) 2980, 1962, 1728; ^1H NMR δ ($CDCl_3$) 1.11 (t, J = 7.3 Hz, Me), 1.30 (t, J = 7.2 Hz, OCH_2CH_3), 2.26 (m, CH_2), 4.26 (q, J = 7.2 Hz, OCH_2CH_3), 5.77 (t, J = 7.2 Hz, CH); ^{13}C NMR ($CDCl_3$) δ 12.4, 14.1, 21.2, 62.5, 103.1, 162.0, 217.7.

***O*-Acyl Phosphonium Salt 25.** Acetyl chloride (1 equiv) was added to a $CDCl_3$ (0.5 mL) solution of PPh_3CBrCO_2Et (0.2 mM) in an NMR tube. After 80 min, the ^1H NMR spectrum revealed PPh_3CBrCO_2Et, bromo phosphonium salt **23b**, and the *O*-acyl phosphonium salt **25** in a ratio of 1:1:1. Data for **25**: ^1H NMR δ 0.65 (t, J = 7.1 Hz, OCH_2CH_3), 2.46 (s, COMe), 3.72 (q, J = 7.1 Hz, OCH_2CH_3), 7.50 (br m, arom). Data for **23b** and for **23a**.

Acetylenic Diester 26. PPh_3CBrCO_2Et (150 mg, 0.36 mmol) was added to an ice-cooled, stirred solution of 3-((diphenylmethoxy)carbonyl)propionyl chloride (prepared[10] from 0.18 mmol of 3-((diphenylmethoxy)carbonyl)propionic acid) in CH_2Cl_2 (5 mL). After 30 min the solution was warmed to 20 °C and the solvent was removed. The residue was purified by chromatography on a 2-mm silica chromatotron plate, eluting with CH_2Cl_2, to give the acetylene diester **26** (47%), which was not purified further: ^1H NMR δ ($CDCl_3$) 1.33 (t, J = 7.0 Hz, OCH_2CH_3), 4.27 (q, J = 7.0 Hz, OCH_2CH_3), 6.59 and 6.85 (AB q, J = 16.0 Hz, CHCH), 6.88 (s, $CHPh_2$), 7.26–7.37 (m, arom); ^{13}C NMR ($CDCl_3$) δ 13.9, 62.5, 76.5, 122.3, 126.0, 126.3, 127.5, 137.5, 149.1, 155.8, 167.9; HRMS calcd for $C_{21}H_{18}O_4$ 334.1205, found 334.1281.

Supplementary Material Available: ^1H NMR spectra of new compounds for which elemental analyses were not obtained (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.